Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MICHAEL NAESBY

Appeal No. 2002-1869
Application No. 09/137,822

ON BRIEF

Before SCHEINER, GRIMES, and GREEN, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 31-85, all of the claims remaining. Claim 55 is representative and reads as follows:

> 55. A triple stranded complex comprising a nucleic acid A, a nucleic acid A binding probe B, said nucleic acid A binding probe B having a base sequence and a binding region which binds to nucleic acid A, and one or more nucleic acid A binding probes C wherein said one or more nucleic acid A binding probes C, in the aggregate, comprise a base sequence different from the sequence of nucleic acid A binding probe B and an aggregate binding region wherein said aggregate binding region, which binds to nucleic acid A, is longer as compared with the binding region of nucleic acid A binding probe B.

The examiner relies on the following reference:

Svinarchuk et al. (Svinarchuk) "An Unusually Stable Purine(Purine-Pyrimidine) Short Triplex," J. Biol. Chem., Vol. 270, No. 23, pp. 14068-14071 (1995)

Claims 31-85 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description.

Claims 31-85 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite.

Claims 31, 32, 34-36, 42, 43, 55, 56, 58, 63, 64, 69, 70, and 72 stand rejected under 35 U.S.C. § 102(b) as anticipated by Svinarchuk.

We reverse the written description and indefiniteness rejections but affirm the anticipation rejection.

Background

The specification discloses a method of detecting a target nucleic acid in a sample by forming and detecting a triple-stranded complex; the target nucleic acid makes up one strand of the triple-stranded complex and is referred to in the specification as "nucleic acid A." See page 3. The other two strands are referred to in the specification as "nucleic acid A binding molecule B" and "nucleic acid A binding molecule C." See id.

According to the specification, a "nucleic acid binding molecule" suitable for use in the disclosed method is

> a molecule recognizing a sequence of nucleobases on nucleic acid A through hydrogen bonding as generally known from the natural recognition of nucleobases in double-stranded nucleic acids, like between the bases A and T or U and between C and G. . . . Those hydrogen bonding moieties are attached to a backbone

> in a consecutive way, such that binding can occur. Suitable backbones are the naturally occurring phosphate sugar backbone (like in nucleic acids, DNA and RNA) and any non-naturally occurring backbones (like in peptide nucleic acids (PNA)).

Pages 5-6.

Nucleic acid binding molecule C binds to nucleic acid A by the usual, Watson-Crick base pairing. See the specification, pages 3 and 15. The binding of molecule C to nucleic acid A forms a duplex region, to which nucleic acid binding molecule B binds (via Hoogsteen binding), forming a triple-stranded structure. See pages 3 and 15. The end result is "controlled binding of a short triplex-forming oligomer (B) under conditions where it will not, by itself, form stable hybrids with a nucleic acid (A), through the controlled binding of one or more, duplex forming, mixed sequence oligomers (C)." Specification, page 3.

The specification discloses an alternative embodiment, using two duplex-forming molecules C to stabilize a triplex-forming molecule B. See, e.g., page 16, last paragraph. The two C molecules, for example, can bind adjacent to each other and thereby form a continuous duplex region to which molecule B can bind. See page 17. The two C molecules are referred to as C1 and C2. The specification states that when

> two independent probes C1 and C2 are used, there is no strict requirement that the triple strand binding region of B is smaller than molecules C. Instead of this, the requirement is that the triple strand binding region of B is smaller than the overall length of the binding region of molecules C1 and C2. The triple stranded binding regions of each of the molecules C1 and C2 are generally smaller than the triple strand binding region of B.

Page 18.

The specification's Example 1 shows formation of triplex structures from a 12-mer DNA molecule (nucleic acid A), a 12-mer PNA molecule complementary to A (molecule C), and a 6-mer PNA molecule (molecule B). See pages 25-27. The data are reported to show that under "appropriate conditions of hybridization, a short PNA oligo (B) will bind to the analyte (A) via Hoogsteen basepairing only when stabilized by another, longer PNA oligo [(C)] binding to the analyte (A) by Watson-Crick basepairing." Page 25.

Discussion

Claim 55 is directed to a triple-stranded complex comprising a target nucleic acid (A), a "nucleic acid A binding probe B", and "one or more nucleic acid A binding probes C". The claim requires that probe B has a different base sequence from that of probes C "in the aggregate" and that the "aggregate binding region" of probes C, i.e., the region that binds to nucleic acid A, is longer than the region of probe B that binds to nucleic acid A. The other claims on appeal either depend on claim 55 or are directed to methods of making or using the complex defined by claim 55. The examiner rejected all of the claims as indefinite and inadequately described, and rejected some of the claims as anticipated.

1. Definiteness and Written Description

The examiner's description and indefiniteness rejections are best understood when they are considered together. The examiner rejected the claims as lacking an adequate description, on the basis that the specification

does not adequately describe the claim limitations "the aggregate" and "aggregate binding regions". See the Examiner's Answer, page 4:

> [T]he specification does not describe or discus[s] "aggregates". Instead the specification describes a triple stranded binding region with two independent probes C1 and C2 (pg. 18). This description does not support aggregate. The definition of aggregate recognized in Stedman's dictionary as "aggregate" is "to unite or come together in a mass or cluster." However, this definition sheds little light on the intended meaning of both "the aggregate" and "aggregate binding regions" as it pertains to the claimed invention. The concept of "forming aggregates" does not appear to be part of the originally filed invention. Therefore, "aggregate" constitutes new matter.

The examiner also rejected the claims as indefinite, based on the following rationales, reproduced from the Examiner's Answer in their entirety:

> Claims 31-85 are indefinite over the recitation of "in the aggregate" because "in the aggregate" lacks antecedent basis.
>
> . . .
>
> Claims 31-85 are indefinite over the recitation of "an aggregate binding region" because it is unclear what "an aggregate binding region" includes. It is unclear whether the aggregate binding region is located on A or C. Further, it is unclear what physical and chemical feature[s] define the aggregate binding region.

Pages 5-6.

Appellant argues that, although the specification does not use the word "aggregate", it adequately describes the claimed invention. Appellant provided his own dictionary excerpt, in which "aggregate" was defined to mean, among other things, "a total or whole considered with reference to its constituent parts." See the Appeal Brief, page 9. Appellant points to pages 17-18 of the specification, in particular, as providing support for the "aggregate" claim limitations, given the foregoing definition. See id.

Appellant also argues that the claims are not indefinite. Appellant points to page 18 of the specification, among other parts, as showing that those skilled in the art would understand the claims' reference to "in the aggregate" to mean "in total" and would understand an "aggregate binding region" to be the complete binding region formed by multiple C molecules. See the Appeal Brief, pages 10-13.

To satisfy the written description requirement, the disclosure as originally filed must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. See Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000). However, the disclosure need not describe the claimed invention using the same words as the claims. See id.

In this case, we agree with Appellant that the specification adequately describes the claimed invention, including its "aggregate" limitations. As the examiner noted, the specification does not disclose the concept of nucleic acids forming an aggregate or cluster. What the specification does disclose is that, when

> two independent probes C1 and C2 are used, there is no strict requirement that the triple strand binding region of B is smaller than molecules C. Instead of this, the requirement is that the triple strand binding region of B is smaller than the overall length of the binding region of molecules C1 and C2. The triple stranded binding regions of each of the molecules C1 and C2 are generally smaller than the triple strand binding region of B.

Page 18.

The corresponding language in claim 55 states that the "one or more . . . binding probes C, in the aggregate, comprise a base sequence different from . . . probe B and an aggregate binding region . . . [that] is longer as compared with the binding region of . . . probe B." We find no difficulty in saying that this claim language is adequately supported by the quoted passage from page 18 of the specification. The examiner's difficulty seems to arise from limiting the possible meaning of "aggregate" only to the meaning quoted in the Examiner's Answer. That definition is not appropriate for the claims. In the context defined by the claims, Appellant's definition of "aggregate" is the more appropriate one. The claim language simply means that the binding probes C, all together, have a different base sequence from probe B and a collectively longer binding region. So interpreted, the claim limitations are adequately described in the specification.

We also agree with Appellant that the claims are not indefinite. "The standard of indefiniteness is somewhat high; a claim is not indefinite merely because its scope is not ascertainable from the face of the claims." Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1342, 65 USPQ2d 1385, 1406 (Fed. Cir. 2003). See also In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971) ("The definiteness of the language employed must be analyzed—not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art.").

The examiner rejected the claims on the basis, first, that the phrase "in the aggregate" lacks antecedent basis. This basis of the rejection makes sense only

if the term "aggregate" is given the narrow definition the examiner ascribed to it. That is, the claims refer to "binding probes C, in the aggregate"; this, in the examiner's view, can only mean that the binding probes C are within some kind of aggregate or cluster. The examiner apparently reasoned that the claims do not define a probe-containing aggregate or cluster, and therefore the term "in the aggregate" lacks antecedent basis.

We have already concluded that the claim term "aggregate" should be construed according to Appellant's definition, i.e., to mean "total" or "collectively". When the claim language is properly interpreted in light of the specification, the claims are not indefinite. This basis of the rejection is reversed.

The examiner also rejected the claims on the basis that the term "aggregate binding region" is indefinite. This basis also seems to relate back to the examiner's incorrect definition of the term "aggregate". Undoubtedly, the claim term "aggregate binding region" would be confusing if it meant "a region that binds an aggregate or cluster": the specification does not even hint at nucleic acids having such a property. When the claim term is given its proper definition, however, it is easily understood to mean the collective binding region of the duplex-forming probes C. See, e.g., the specification at page 18 (referring to the "overall length of the binding region of molecules C1 and C2"). This basis of the rejection is also reversed.

2. Anticipation

The examiner rejected claims 31, 32, 34-46, 42, 43, 55, 56, 58, 63, 64, 69, 70, and 72 under 35 U.S.C. § 102(b). Appellant argued these claims as a group with respect to the anticipation rejection. See the Appeal Brief, pages 15-17. Therefore, they stand or fall together. See In re Kaslow, 707 F.2d 1366, 1376, 217 USPQ 1089, 1096 (Fed. Cir. 1983) ("Since the claims are not separately argued, they all stand or fall together.").

We will consider claim 55 as representative of the rejected claims. Claim 55 is directed to a triple-stranded complex comprising a target nucleic acid (A), a "nucleic acid A binding probe B", and at least one "nucleic acid A binding probes C". The claim requires that probe B and probe(s) C have different base sequences and that the collective binding region of probe(s) C is longer than that of probe B.

The examiner rejected claim 55, among others, as anticipated by Svinarchuk. Svinarchuk discloses forming a triple-stranded complex as part of a co-migration assay. See page 14068, right-hand column: a 242-bp, double-stranded DNA fragment was incubated with a ^{32}P-labeled, 13-bp oligonucleotide under conditions that allowed formation of a triple helix. Svinarchuk discloses that the smaller oligonucleotide bound to the double-stranded DNA to form a triplex structure that increased the stability of the double-stranded DNA. See the abstract. See also page 14069, first paragraph under "Results": the interaction was specific to DNA containing the target sequence and was of high stability.

The triple-stranded DNA complex disclosed by Svinarchuk meets all of the limitations of claim 55. It is a triple-stranded complex, comprising a nucleic acid A (one strand of the 242-bp fragment), a nucleic acid A binding probe B (the 13-bp oligo), and a nucleic acid A binding probe C (the other strand of the 242-bp fragment). The binding probe C has a base sequence different from that of binding probe B (a 242-bp sequence is different from a 13-bp sequence), and binding probe C has a longer binding region (242 bp) than does binding probe B (13 bp).

Appellant argues that Svinarchuk does not anticipate the instant claims because Svinarchuk's complex does not comprise at least two probes, as required by the claims. Appellant cites a dictionary definition of "probe" as meaning "a substance (as DNA in genetic research) used to obtain specific information for diagnostic or experimental purposes." Appeal Brief, page 16. Appellant argues that Svinarchuk's complex comprises only a single "probe" and therefore does not meet all of the instant claim limitations. See id., pages 16-17; Reply Brief, pages 11-13.

This argument is not persuasive. "It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art." In re Sneed, 710 F.2d 1544,1548, 218 USPQ 385, 388 (Fed. Cir. 1983) (citation omitted).

The specification provides no definition of "probes" that would distinguish the claimed complex from that disclosed by Svinarchuk. The specification makes clear that both molecules B and C, as well as molecule A, can be naturally occurring DNA. See page 14: "The molecular structure of nucleic acid binding molecules B and C (apart from the sequence requirements) can generally be the same or different. However, it is much preferred that at least one of molecules B and C is a nucleic acid binding compound comprising a non-naturally occurring backbone." Since it is only "much preferred" that B and/or C have non-naturally occurring backbones, it follows that that property is not required. Thus, both B and C can be naturally occurring DNA, as disclosed by Svinarchuk.

The specification also makes clear that calling a molecule a "probe" does not imply that the molecule has any special properties. See page 14 again: "In the following[,] molecules B and C are referred to as probes." The compounds are the same whether they are called "molecules" or "probes".

The examiner made this point in the Answer. See page 9: "'[P]robe does not confer any size limitation or structural characteristics. . . . A probe is simply a piece of nucleic acid and the art teaches nucleic acid may be used as a probe. . . . Thus[,] probe in the sense that it is used to 'interrogate or explore in order to obtain information about the object of the investigation' is an intended use which does not carry weight."

Appellant has also not adequately explained how the complex that they disclose and claim includes two "probes" (i.e., two molecules that are used to obtain specific information for diagnostic or experimental purposes), while the

complex disclosed by Svinarchuk has only one. Appellant argues that "the triplex of Svinarchuk et al. is a composition formed from a double-stranded target nucleic acid (e.g. [sic, i.e.], nucleic acid analyte) and a single probe. By comparison, the triplex of the claimed invention comprises at least two probes and one strand of nucleic acid analyte." Reply Brief, page 12 n. 10.

This asserted difference, however, is merely semantic. In both cases, a small oligonucleotide binds to a length of double-stranded nucleic acid to form a triple-stranded structure, and the formation of the triple-stranded structure is detected. Whether you start with single-stranded DNA, make it double-stranded, then bind a triplex-forming oligo (as in the specification), or start with double-stranded DNA and bind a triplex-forming oligonucleotide (as in Svinarchuk), the same complex results.

Our conclusion is reinforced by the specification's Example 1. In that example, the target nucleic acid and the binding molecule (or probe) C are the same length. Thus, just as in Svinarchuk, the two molecules would be expected to hybridize, through Watson-Crick base-pairing, along their entire length and form a double-stranded molecule. The smaller binding molecule (or probe) B would then be expected to bind to the double-stranded complex via Hoogsteen binding, and form a triple-stranded structure, like that of Svinarchuk. Example 1 therefore confirms our conclusion that claim 55 reads on the complex disclosed by Svinarchuk.

Summary

We reverse the rejections based on 35 U.S.C. § 112, first and second paragraphs, because the specification adequately defines and describes the disputed claim terms. However, we affirm the rejection based on 35 U.S.C. § 102(b) because the complex of claim 55 is identically disclosed by Svinarchuk. Claims 31, 32, 34-36, 42, 43, 56, 58, 63, 64, 69, 70, and 72 fall with claim 55. Thus, claims 33, 37-41, 44-54, 57, 59-62, 65-68, 71, and 73-85 are not subject to any outstanding rejection.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED IN PART

Toni R. Scheiner)
Administrative Patent Judge)
)
)
) BOARD OF PATENT
Eric Grimes)
Administrative Patent Judge) APPEALS AND
)
) INTERFERENCES
)
Lora M. Green)
Administrative Patent Judge)

EG/dym

Arent, Fox, Kintner, Plotkin & Kahn
1050 Connecticut Avenue, N.W.
Suite 600
Washington, DC 20036